

# Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/id/eprint/115888/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Zhao, Yingjie, Guo, Tingwei, Fiksinski, Ania, Breetvelt, Elemei, McDonald-McGinn, Donna M., Crowley, Terrence B., Diacou, Alexander, Schneider, Maude, Eliez, Stephan, Swillen, Ann, Breckpot, Jeroen, Vermeesch, Joris, Chow, Eva W. C., Gothelf, Doron, Duijff, Sasja, Evers, Rens, van Amelsvoort, Thérèse A., Van Den Bree, Marianne ORCID: <https://orcid.org/0000-0002-4426-3254>, Owen, Michael ORCID: <https://orcid.org/0000-0003-4798-0862>, Niarchou, Maria ORCID: <https://orcid.org/0000-0002-8855-7393>, Bearden, Carrie E., Ornstein, Claudia, Pontillo, Maria, Buzzanca, Antonino, Vicari, Stefano, Armando, Marco, Murphy, Kieran C., Murphy, Clodagh, Garcia-Minaur, Sixto, Philip, Nicole, Campbell, Linda, Morey-Cañellas, Jaume, Raventos, Jasna, Rosell, Jordi, Heine-Suner, Damian, Shprintzen, Robert J., Gur, Raquel E., Zackai, Elaine, Emanuel, Beverly S., Wang, Tao, Kates, Wendy R., Bassett, Anne S., Vorstman, Jacob A. S., Morrow, Bernice E., International 22q11.2, Brain and Behavior Consortium and Chawner, Samuel 2018. Variance of IQ is partially dependent on deletion type among 1,427 22q11.2 deletion syndrome subjects. American Journal of Medical Genetics Part A 176 (10) , pp. 2172-2181. 10.1002/ajmg.a.40359 file

Publishers page: <http://dx.doi.org/10.1002/ajmg.a.40359>  
<<http://dx.doi.org/10.1002/ajmg.a.40359>>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies.

See

<http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



# **Variance of IQ is partially dependent on deletion type among 1,427 22q11.2 deletion syndrome subjects**

## ***Human genetics***

Yingjie Zhao<sup>1</sup>, Tingwei Guo<sup>1</sup>, Ania Fiksinski<sup>2,7</sup>, Elemi Breetvelt<sup>7</sup>, Donna M. McDonald-McGinn<sup>4</sup>, Terrence B. Crowley<sup>4</sup>, Alexander Diacou<sup>1</sup>, Maude Schneider<sup>5</sup>, Stephan Eliez<sup>5</sup>, Ann Swillen<sup>6</sup>, Jeroen Breckpot<sup>6</sup>, Joris Vermeesch<sup>6</sup>, Eva W. C. Chow<sup>7</sup>, Doron Gothelf<sup>9,10</sup>, Sasja Duijff<sup>2</sup>, Rens Evers<sup>11</sup>, Thérèse A. van Amelsvoort<sup>11</sup>, Marianne van den Bree<sup>12</sup>, Michael Owen<sup>12</sup>, Maria Niarchou<sup>12</sup>, Carrie E. Bearden<sup>13</sup>, Claudia Ornstein<sup>14</sup>, Maria Pontillo<sup>5</sup>, Antonino Buzzanca<sup>15</sup>, Stefano Vicari<sup>5</sup>, Marco Armando<sup>5,16</sup>, Kieran C. Murphy<sup>17</sup>, Clodagh Murphy<sup>18</sup>, Sixto Garcia-Minaur<sup>19</sup>, Nicole Philip<sup>20</sup>, Linda Campbell<sup>21</sup>, Jaume Morey<sup>22</sup>, Jasna Raventos<sup>22</sup>, Jordi Rosell<sup>22</sup>, Damian Heine-Suner<sup>22</sup>, Robert J. Shprintzen<sup>23</sup>, Raquel E. Gur<sup>24</sup>, Elaine Zackai<sup>4</sup>, Beverly S. Emanuel<sup>4</sup>, Tao Wang<sup>25</sup>, Wendy R. Kates<sup>26</sup>, Anne S. Bassett<sup>7,8</sup>, Jacob A. S. Vorstman<sup>3</sup>, Bernice E. Morrow<sup>1\*</sup> on behalf of the International 22q11.2 Brain and Behavior Consortium<sup>27</sup>

<sup>1</sup>Department of Genetics, Albert Einstein College of Medicine, Bronx, NY, USA

<sup>2</sup>Department of Psychiatry, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, the Netherlands

<sup>3</sup>Department of Psychiatry, Hospital for Sick Children, Toronto, Canada

<sup>4</sup>Division of Human Genetics, Children's Hospital of Philadelphia and Department of Pediatrics,  
Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA

<sup>5</sup>Developmental Imaging and Psychopathology Lab, University of Geneva School of Medicine, Geneva,  
Switzerland

<sup>6</sup>Center for Human Genetics, Katholieke Universiteit Leuven (KU Leuven), Leuven, Belgium

<sup>7</sup>Center for Addiction and Mental Health, Toronto General Hospital and the University of Toronto,  
Toronto, Canada

<sup>8</sup>The Dalglish 22q Clinic for Adults, Toronto General Hospital, University Health Network, Toronto,  
Canada

<sup>9</sup>Sackler Faculty of Medicine and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel

<sup>10</sup>The Child Psychiatry Division, Edmond and Lily Sapfira Children's Hospital, Sheba Medical Center,  
Ramat Gan, Israel

<sup>11</sup>Department of Psychiatry and Psychology, Maastricht University, Maastricht, The Netherlands

<sup>12</sup>MRC Centre for Neuropsychiatric Genetics and Genomics, Division of Psychological Medicine and Clinical Neuroscience, Cardiff University, Cardiff, Wales, UK

<sup>13</sup>Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, Los Angeles, CA, USA

<sup>14</sup>Department of Psychiatry, Hospital Clinico Universidad de Chile, Santiago, Chile

<sup>15</sup>Department of Human Neuroscience, University Sapienza of Rome, Rome, Italy

<sup>16</sup>Child and Adolescence Neuropsychiatry Unit, Department of Neuroscience, Children Hospital Bambino Gesù, Rome, Italy

<sup>17</sup>Department of Psychiatry, Royal College of Surgeons in Ireland, Dublin, Ireland

<sup>18</sup>Department of Psychiatry, King's College London, London, England

<sup>19</sup>Section of Clinical Genetics and Dismorphology, Instituto de Genética Médica y Molecular, INGEMM, Hospital Universitario La Paz, Madrid, Spain

<sup>20</sup>Department of Medical Genetics, APHM, MMG, INSERM, Aix-Marseille University, Marseille, France

<sup>21</sup>School of Psychology, University of Newcastle, Newcastle, Australia

<sup>22</sup>Section of Genetics, Hospital Son Espases, Palma, Spain

<sup>23</sup>The Virtual Center for Velo-Cardio-Facial Syndrome and Related Disorders, Syracuse, NY, USA

<sup>24</sup>Department of Psychiatry, Perelman School of Medicine of the University of Pennsylvania,  
Philadelphia, USA

<sup>25</sup>Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY,  
USA

<sup>26</sup>Department of Psychiatry and Behavioral Sciences, and Program in Neuroscience, SUNY Upstate  
Medical University, Syracuse, USA

<sup>27</sup>Members of the International Chromosome 22q11.2 Consortium that participated in this study and all  
members of the International 22q11.2 Brain and Behavior Consortium (IBBC) are provided in Table S1

\*Corresponding Author: Bernice E. Morrow, Department of Genetics, Albert Einstein College of  
Medicine, 1301 Morris Park Ave, Bronx NY 10461, Email: [Bernice.morrow@einstein.yu.edu](mailto:Bernice.morrow@einstein.yu.edu)

Phone: 718-678-1121, Fax: 718-678-1016

**Supplementary Table 1.** Full list of contributing authors as part of the International 22q11.2 Brain and Behavior

Last Name	First Name	Department	Institution	City, State, Country	Email
Antonarakis†	Stylios, E.	Department of Genetic Medicine and Development	University of Geneva Medical School and University Hospitals of Geneva	Geneva, Switzerland	Stylios.Antonarakis@unige.ch
Antshel*	Kevin	Department of Psychology	SUNY Upstate Medical University	Syracuse, NY, USA	kmantshe@syr.edu
Arango*	Celso	Department of Child and Adolescent Psychiatry	Hospital General Universitario Gregorio Marañón. Universidad Complutense Madrid	Madrid, Spain	carango@hggm.es
Armando*	Marco	Developmental Imaging and Psychopathology Lab, Department of Psychiatry	School of Medicine, University of Geneva	Geneva, Switzerland	marco.armando@unige.ch
Bassett*	Anne, S.	Dalglish Family 22q Clinic, Clinical Genetics Research Program and Department of Psychiatry	Toronto General Hospital, Centre for Addiction and Mental Health, and the University of Toronto	Toronto, Canada	anne.bassett@utoronto.ca
Bearden*	Carrie, E.	Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior	University of California, Los Angeles	Los Angeles, CA, USA	cbearden@mednet.ucla.edu
Biondi*	Massimo	Department of Neurology and Psychiatry	Sapienza University	Rome, Italy	massimo.biondi@uniroma1.it
Blonska†	Anna	Department of Genetics	Albert Einstein College of Medicine	Bronx, NY, USA	an.blonska@gmail.com
Boot*	Erik	Dalglish Family 22q Clinic	Toronto General Hospital	Toronto, Canada	erik.boot@uhn.ca
Bravo-Sanchez*	Marta	Institute of Medical and Molecular Genetics (INGEMM),	Hospital General Universitario Gregorio Marañón	Madrid, Spain	marta.bravo@salud.madrid.org
Breckpot†	Jeroen	Center for Human Genetics	Katholieke University, Leuven	Leuven, Belgium	jeroen.breckpot@uzleuven.be
Breetvelt*	Elemi	Dalglish Family 22q Clinic and Clinical Genetics Research Program,	Toronto General Hospital, University Health Network and Centre for Addiction and Mental Health	Toronto, Canada	Elemi.Breetvelt@uhn.ca

Last Name	First Name	Department	Institution	City, State, Country	Email
Busa*	Tiffany	Department of Medical Genetics	Aix-Marseille University	Marseille, France	tiffany.busa@ap-hm.fr
Butcher*	Nancy	Clinical Genetics Research Program	Centre for Addiction and Mental Health	Toronto, Canada	nancy.j.butcher@gmail.com
Buzzanca*	Antonino	Department of Neurology and Psychiatry	Sapienza University	Rome, Italy	antonino.buzzanca@uniroma1.it
Calkins*	Monica	Department of Psychiatry	Perelman School of Medicine of the University of Pennsylvania	Philadelphia, PA, USA	mcalkins@penmedicine.upenn.edu
Campbell*	Linda	School of Psychology	University of Newcastle	Newcastle, Australia	linda.e.campbell@newcastle.edu.au
Carmel*	Miri	Felsenstein Medical Research Center, Sackler Faculty of Medicine	Tel Aviv University and Felsenstein Medical Research Center	Tel Aviv, Petah Tikva, Israel	mcarmel@post.tau.ac.il
Chawner*	Samuel	Psychological Medicine and Clinical Neuroscience	Cardiff University	Cardiff, Wales, UK	ChawnerSJ@cardiff.ac.uk
Chow*	Eva	Clinical Genetics Research Program and Department of Psychiatry	Centre for Addiction and Mental Health and the University of Toronto	Toronto, Canada	eva.chow@utoronto.ca
Coleman†	Karlene	Marcus Autism Center	Children's Healthcare of Atlanta	Atlanta, GA, USA	kcole05@emory.edu
Crowley*	Terence Blaine	Division of Human Genetics	The Children's Hospital of Philadelphia	Philadelphia, PA, USA	crowleyt@email.chop.edu
Cubells*	Joseph	Department of Human Genetics	Emory University	Atlanta, GA, USA	jcubell@emory.edu
Cutler*	David	Department of Human Genetics	Emory University	Atlanta, GA, USA	djcutle@emory.edu
Dallapiccola†	Bruno	Department of Medical Genetics	Bambino Gesù Hospital, Rome	Rome, Italy	bruno.dallapiccola@opbg.net
Demaerel*	Wolfram	Center for Human Genetics	Katholieke University, Leuven	Leuven, Belgium	wolfram.demaerel@med.kuleuven.be
Devriendt†	Koen	Center for Human Genetics	Katholieke University, Leuven	Leuven, Belgium	koenraad.devriendt@uzleuven.be
Diacou*	Alexander	Department of Genetics	Albert Einstein College of Medicine	Bronx, NY, USA	alexander.diacou@einstein.yu.edu
Di Fabio*	Fabio	Department of Psychiatry	Sapienza University	Rome, Italy	fabiodifa@gmail.com
Digilio*	Maria Cristina	Department of Medical Genetics	Ospedale Bambino Gesù	Rome, Italy	Mcristina.digilio@opbg.net

<b>Last Name</b>	<b>First Name</b>	<b>Department</b>	<b>Institution</b>	<b>City, State, Country</b>	<b>Email</b>
Duijff*	Sasja	Department of Psychiatry, Brain Center Rudolf Magnus,	University Medical Center Utrecht	Utrecht, the Netherlands	s.duijff@umcutrecht.nl
Eliez*	Stephan	Developmental Imaging and Psychopathology Lab	University of Geneva	Geneva, Switzerland	Stephan.eliez@etat.ge.ch
Emanuel*	Beverly, S.	Division of Human Genetics	The Children's Hospital of Philadelphia and the Perelman School of Medicine of the University of Pennsylvania	Philadelphia, PA, USA	emanuel@email.chop.edu
Epstein*	Michael	Department of Human Genetics	Emory University	Atlanta, GA, USA	mpepste@emory.edu
Evers*	Rens	Department of Psychiatry and Psychology	Maastricht University	Maastricht, the Netherlands	revers@koraalgroep.nl
Fernandez Garcia-Moya*	Luis	Institute of Genetics and Molecular	Hospital Universitario La Paz	Madrid, Spain	lfernandezg@salud.madrid.org
Fiksinski*	Ania	Department of Psychiatry, Brain Center Rudolf Magnus,	Department of Psychiatry, Brain Center Rudolf Magnus, University Medical Center Utrecht	Utrecht, the Netherlands	a.m.fiksinski@umcutrecht.nl
Fraguas*	David	Institute of Medical and Molecular Genetics (INGEMM),	Hospital General Universitario Gregorio Marañón and CIBERSAM	Madrid, Spain	davidfraguas@gmail.com
Fremont*	Wanda	Department of Psychiatry and Behavioral Sciences	SUNY Upstate Medical University	Syracuse, NY, USA	fremontw@upstate.edu
Fritsch*	Rosemarie	Department of Psychiatry	Hospital Clinico Universidad de Chile	Santiago, Chile	Fritsch.rosemarie@gmail.com
Garcia-Minaur*	Sixto	Section of Clinical Genetics and Dismorphology	Instituto de Genética Médica y Molecular, Hospital Universitario La Paz	Madrid, Spain	sixto.garciamin@gmail.com
Golden*	Aaron	Department of Genetics, Bioinformatics and Biostatistics Research Center	Albert Einstein College of Medicine and National University of Ireland, Galway	New York, USA and Galway, Ireland	aaron.golden@nuigalway.ie



Last Name	First Name	Department	Institution	City, State, Country	Email
Gothelf*	Doron	The Child Psychiatry Unit, Edmond and Lily Saffra Children's Hospital, Sackler Faculty of Medicine	Tel Aviv University and Sheba Medical Center	Tel Aviv, Israel	gothelf@post.tau.ac.il
Guo*	Tingwei	Department of Genetics	Albert Einstein College of Medicine	Bronx, NY, USA	Tingwei.guo@einstein.yu.edu
Gur*	Ruben	Department of Psychiatry	Perelman School of Medicine of the University of Pennsylvania	Philadelphia, PA, USA	gur@pennmedicine.upenn.edu
Gur*	Raquel, E.	Department of Psychiatry and the Lifespan Brain Institute	Perelman School of Medicine and Children's Hospital of Philadelphia	Philadelphia, USA	raquel@pennmedicine.upenn.edu
Heine-Suner*	Damian	Section of Genetics	Hospital Son Espases	Palma, Spain	damian.heine@ssib.es
Hestand*	Matthew	Center for Human Genetics and Division of Human Genetics	Katholieke University, Leuven and Cincinnati Children's Hospital Medical Center	Leuven, Belgium and Cincinnati, OH, USA	matthew.hestand@cchmc.org
Heung	Tracy	Dalglish Family 22q Clinic, Clinical Genetics Research Program and Department of Psychiatry	Toronto General Hospital, Centre for Addiction and Mental Health, and the University of Toronto	Toronto, Canada	Tracy.Heung@camh.ca
Hooper*	Stephen	Department of Allied Health Sciences	Duke University and the University of North Carolina at Chapel Hill Medical Center	Durham, USA and Chapel Hill, USA	stephen_hooper@med.unc.edu
Johnston*	H. Richard	Department of Human Genetics, Biostatistics and Bioinformatics	Emory University School of Medicine, Rollins School of Public Health	Atlanta, GA, USA	henry.johnston@gmail.com
Kates*	Wendy	Department of Psychiatry and Behavioral Sciences, and Program in Neuroscience	SUNY Upstate Medical University	Syracuse, USA	katesw@upstate.edu
Kushan-Wells*	Leila	Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior	University of California, Los Angeles	Los Angeles, USA	lkushan@mednet.ucla.edu
Laorden-Nieto*	Alejandra	Department of Child and Adolescent Psychiatry	Hospital General Universitario Gregorio Marañón	Madrid, Spain	ale.teresalaorden@gmail.com
Lattanzi*	Guido	Department of Neurology and Psychiatry	Sapienza University	Rome, Italy	guido.m.lattanzi@gmail.com

Last Name	First Name	Department	Institution	City, State, Country	Email
Lin*	Jhih-Rong	Department of Genetics	Albert Einstein College of Medicine	New York, USA	jhihrong.lin@gmail.com
Maeder*	Johanna	Developmental Imaging and Psychopathology Lab	University of Geneva	Geneva, Switzerland	Johanna.Maeder@unige.ch
Marino*	Bruno	Department of Pediatrics	La Sapienza University	Rome, Italy	Bruno.marino@uniroma1.it
Marshall*	Christian, R.	Department of Pediatric Laboratory Medicine, Laboratory Medicine and Pathobiology	The Hospital for Sick Children, University of Toronto	Toronto, Canada	crm@sickkids.ca
Mayoral*	Maria	Department of Child and Adolescent Psychiatry	Hospital General Universitario Gregorio Marañón, Universidad Complutense, IISGM, CIBERSAM	Madrid, Spain	maria.mayoral@iisgm.com
McCabe*	Kathryn	School of Psychology	University of Newcastle	Newcastle, Australia	kathryn.mccabe@sydney.edu.au
McDonald-McGinn*	Donna	Division of Human Genetics	The Children's Hospital of Philadelphia and the Perelman School of Medicine of the University of Pennsylvania	Philadelphia, PA, USA	mcginn@email.chop.edu
McGinn	Daniel	Division of Human Genetics	The Children's Hospital of Philadelphia	Philadelphia, PA, USA	mcginnde@email.chop.edu
Michaelovsky*	Elena	Felsenstein Medical Research Center, Sackler Faculty of Medicine	Tel Aviv University and Felsenstein Medical Research Center	Tel Aviv, Petah Tikva, Israel	michaelo@post.tau.ac.il
Morey Cañellas*	Jaume	Belear Institute of Child and Adolescent Psychiatry	Hospital Universitari Son Espases	Palma, Spain	jaume.morey@ssib.es
Morrow*	Bernice, E.	Department of Genetics	Albert Einstein College of Medicine	Bronx, NY, USA	Bernice.Morrow@einstein.yu.edu
Moss*	Edward		The Children's Hospital of Philadelphia	Philadelphia, PA, USA	kidbrains@gmail.com
Moss*	Hayley	Psychological Medicine and Clinical Neuroscience	Cardiff University	Cardiff, Wales, UK	mosshm@cardiff.ac.uk
Mulle*	Jennifer	Department of Human Genetics	Emory University	Atlanta, GA, USA	jmulle@emory.edu
Murphy*	Declan	Department of Psychiatry	King's College London	London, England	declan.murphy@kcl.ac.uk

Last Name	First Name	Department	Institution	City, State, Country	Email
Murphy*	Kieran, C.	Department of Psychiatry	Royal College of Surgeons in Ireland	Dublin, Ireland	kmurphy@rcsi.ie
Murphy*	Clodagh	Department of Psychiatry	King's College London	London, England	clodagh.m.murphy@kcl.ac.uk
Niarchou*	Maria	Psychological Medicine and Clinical Neuroscience	Cardiff University	Cardiff, Wales, UK	niarchoum@cardiff.ac.uk
Owen*	Michael	Psychological Medicine and Clinical Neuroscience	Cardiff University	Cardiff, Wales, UK	owenmj@Cardiff.ac.uk
Philip*	Nicole	Department of Medical Genetics	APHM, MMG, INSERM, Aix-Marseille University	Marseille, France	nicole.philip@ap-hm.fr
Pontillo	Maria	Department of Neuroscience	Bambino Gesù Children's Hospital, IRCCS	Rome, Italy	maria.pontillo@opbg.net
Raventos	Jasna	Secci-de Genetica	Hospital Universitari Son Espases	Palma de Mallorca	Jasna.raventos@ssib.es
Repetto*	Gabriela	Center for Human Genetics	Clinica Alemana Universidad del Desarrollo	Santiago, Chile	grepetto@udd.cl
Rosell†	Jordi	Secci-de Genetica	Hospital Universitari Son Espases	Palma de Mallorca	jordi.rosell@ssib.es
Schneider*	Maude	Developmental Imaging and Psychopathology Lab	University of Geneva	Geneva, Switzerland	maude.schneider@unige.ch
Shashi*	Vandana	Department of Pediatrics	Duke University	Durham, NC, USA	vandana.shashi@duke.edu
Simon*	Tony	M.I.N.D. Institute & Department of Psychiatry and Behavioral Sciences	University of California	Davis, CA, USA	tjsimon@ucdavis.edu
Swillen*	Ann	Center for Human Genetics	Katholieke University, Leuven	Leuven, Belgium	ann.swillen@uzleuven.be
Tang*	Sunny	Department of Psychiatry	Perelman School of Medicine of the University of Pennsylvania	Philadelphia, USA	suntang@pennmedicine.med.upenn.edu
Tassone*	Flora	M.I.N.D. Institute & Department of Biochemistry and Molecular Medicine	University of California	Davis, CA, USA	ftassone@ucdavis.edu
Tomita-Mitchell†	Aoy	Division of Pediatric Cardiovascular Surgery	Children's Hospital of Wisconsin	Milwaukee, WI, USA	amitchell@mcw.edu
Unolt*	Marta	Department of Pediatrics	Ospedale Bambino Gesù and La Sapienza University	Rome, Italy	unolt.marta@gmail.com
van Amelsvoort*	Therese	Department of Psychiatry and Psychology	Maastricht University	Maastricht, the Netherlands	t.vanamelsvoort@maastrichtuniversity.nl

Last Name	First Name	Department	Institution	City, State, Country	Email
van den Bree*	Marianne	Psychological Medicine and Clinical Neuroscience	Cardiff University	Cardiff, Wales, UK	vandenbreemb@cf.ac.uk
van Duin*	Esther, D. A.	Department of Psychiatry and Psychology	Maastricht University	Maastricht, the Netherlands	eda.vanduin@maastrichtuniversity.nl
Vergaelen*	Elfi	Center for Human Genetics	Katholieke University, Leuven	Leuven, Belgium	elfi.vergaelen@uzleuven.be
Vermeesch*	Joris	Center for Human Genetics	Katholieke University, Leuven	Leuven, Belgium	joris.vermeesch@uzleuven.be
Vial†	Cecilia	Center for Genetics and Genomics	Clinica Alemana Universidad del Desarrollo	Santiago, Chile	mcvial@udd.cl
Vicari*	Stefano	Department of Medical Genetics	Ospedale Bambino Gesù	Rome, Italy	stefano.vicari@opbg.net
Vingerhoets*	Claudia	Department of Psychiatry and Psychology	Maastricht University	Maastricht, the Netherlands	claudia.vingerhoets@maastrichtuniversity.nl
Vorstman*	Jacob	Department of Psychiatry, Brain Center Rudolf Magnus,	Department of Psychiatry, Brain Center Rudolf Magnus, University Medical Center Utrecht and the Children's Hospital of Philadelphia	Utrecht, the Netherlands and Philadelphia, PA, USA	j.a.s.vorstman@umcutrecht.nl
Wang*	Tao	Department of Epidemiology & Population Health	Albert Einstein College of Medicine	Bronx, NY, USA	tao.wang@einstein.yu.edu
Warren*	Stephen	Department of Human Genetics	Emory University	Atlanta, GA, USA	swarren@emory.edu
Weinberger*	Ronnie	The Child Psychiatry Unit, Edmond and Lily Sapfra Children's Hospital	Tel Aviv University and Sheba Medical Center	Tel Aviv, Israel	ronnie.wein@gmail.com
Weisman*	Omri	The Child Psychiatry Unit, Edmond and Lily Sapfra Children's Hospital	Tel Aviv University and Sheba Medical Center	Tel Aviv, Israel	omriwei@yahoo.com
Weizman*	Abraham	Felsenstein Medical Research Center	Sackler Faculty of Medicine, Tel Aviv University	Tel Aviv and Petah Tikva, Israel	weizmana@gmail.com
Yingjie*	Zhao	Department of Genetics	Albert Einstein College of Medicine	Bronx, NY, USA	Yingjie.zhao@einstein.yu.edu
Zackai*	Elaine	Division of Human Genetics	The Children's Hospital of Philadelphia	Philadelphia, PA, USA	zackai@email.chop.edu

Zhang*	Zhengdong	Department of Genetics	Albert Einstein College of Medicine	Bronx, NY, USA	zhengdong.zhang@einstein.yu.edu
Zwick*	Michael	Department of Human Genetics	Emory University	Atlanta, GA, USA	mzwick@emory.edu
<p>*IBBC Members and International 22q11.2 Consortium Members</p> <p>† International 22q11.2 Consortium Members that are not part of the IBBC</p>					

**Supplementary Table 2.** Detailed grouping criterion for 21 study sites (no. of sample in parentheses)

Group of study site	Study site included
US and Canada	CHOP/U. Penn, PA(182); Duke U., Durham, NC(55); Emory U., Atlanta, GA(1); Upstate Medical Center, Syracuse, NY(137); UCLA, Los Angeles, CA(62); UC Davis, Davis, CA(58); Toronto, CA(101)
Northern Europe	Geneva, Switzerland(105); Leuven, Belgium(101); Maastricht, Netherlands(79); Utrecht, Netherlands(130)
Southern Europe	Marseille, France(24); Tel Aviv, Israel(81); Madrid, Spain(25); Mallorca, Spain(14); Rome, Italy(52); Santiago, Chile (60)
UK and Australia	Cardiff, Wales(75); Dublin, Ireland(53); London, England(11); Newcastle, Australia(21),

**Supplementary Table 3.** Multivariable linear regression analysis of IQ and deletion size with adjustment of sex and age stratified by group of study site

Study site	deletion type (No of subjects)	FSIQ		VIQ		PIQ	
		$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>
Canada & US	AD (reference,569)						
	AB(27)	1.46	0.247	1.77	0.246	1.3	0.363
Northern Europe	AD (reference,392)						
	AB(23)	5.09	1.59E-4	6.13	9.10E-5	4.9	4.24E-4
Southern Europe	AD (reference,238)						
	AB(18)	1.64	0.378	0.97	0.649	0.378	0.864
UK & Australia	AD (reference,154)						
	AB(6)	5.48	0.054	9.48	0.080	6.924	0.044

**Supplementary Table 4.** Statistical power (%) at  $\alpha=0.05$  under various differences in IQ measures between 22q11.2DS subjects with AD and AB deletions.

Difference (SD)	Power(%)
0.1	15
0.2	45
0.3	79
0.4	95

<sup>a</sup>Standard deviation (SD), PASS software (<http://www.ncss.com/pass.html>) was used for these calculations. In a design of an independent samples t-test, we have about 80% power to detect the IQ difference at 0.3 SD level when the sample size of AD equals to 1,270 and AB equals to 76, which are close to the top two largest deletion groups in our study.

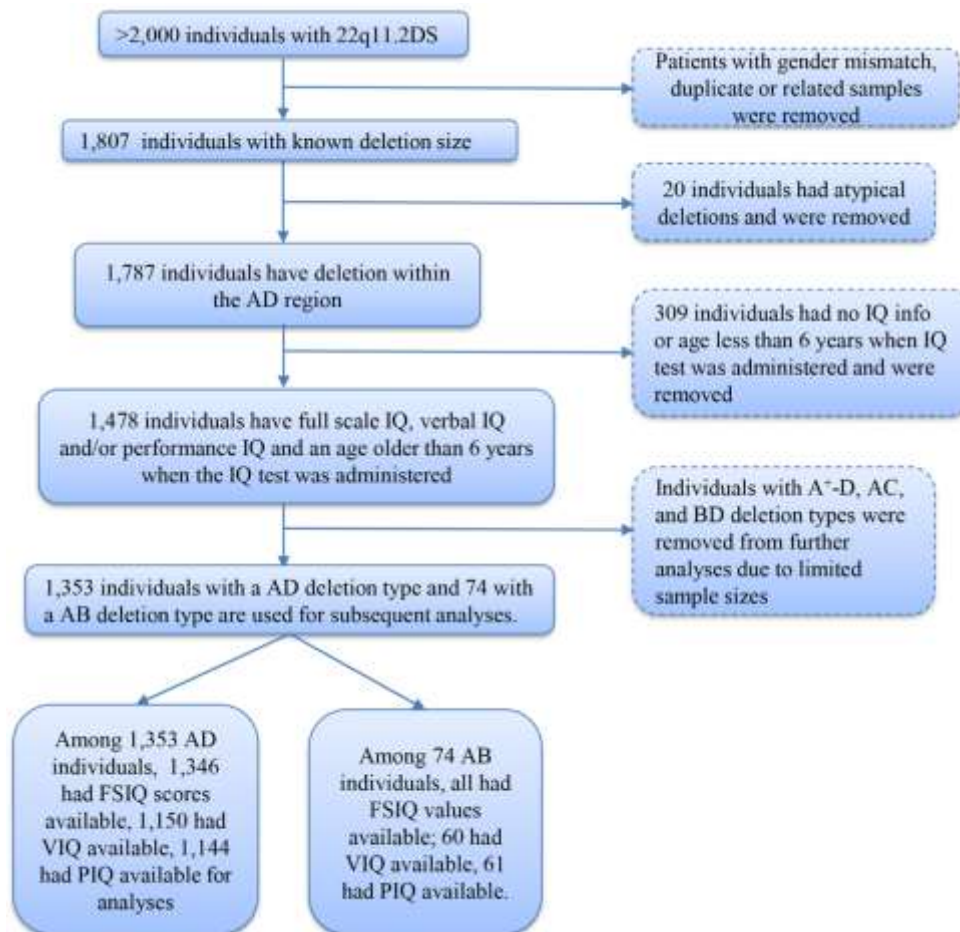
**Supplementary Table 5.** Number of samples with missing values for each variable between AD and AB group and the distribution of each categorical variable between AD and AB group

Total number=1427	AD	AB	<i>P</i> value
<b>Sex</b>			0.722 <sup>a</sup>
Male	647	37	
Female	706	37	
<b>Age</b>	1330	74	
Missing	23	0	
<b>CHD<sup>c</sup></b>			0.566 <sup>a</sup>
Cases	286	17	
Controls	593	30	
Missing	474	26	
<b>FSIQ<sup>d</sup></b>	1346	74	
Missing	7	0	
<b>VIQ<sup>e</sup></b>	1150	60	
Missing	203	14	
<b>PIQ<sup>f</sup></b>	1144	61	
Missing	209	13	
<b>IQ test</b>			0.460 <sup>b</sup>
Wechsler	1306	73	
Non-Wechsler	39	3	
Unknown	8	1	
<b>Study sites</b>			0.381 <sup>a</sup>
US&Canada	569	27	
North_Europe	392	23	
South_Europe	238	18	
UK&Australia	154	6	

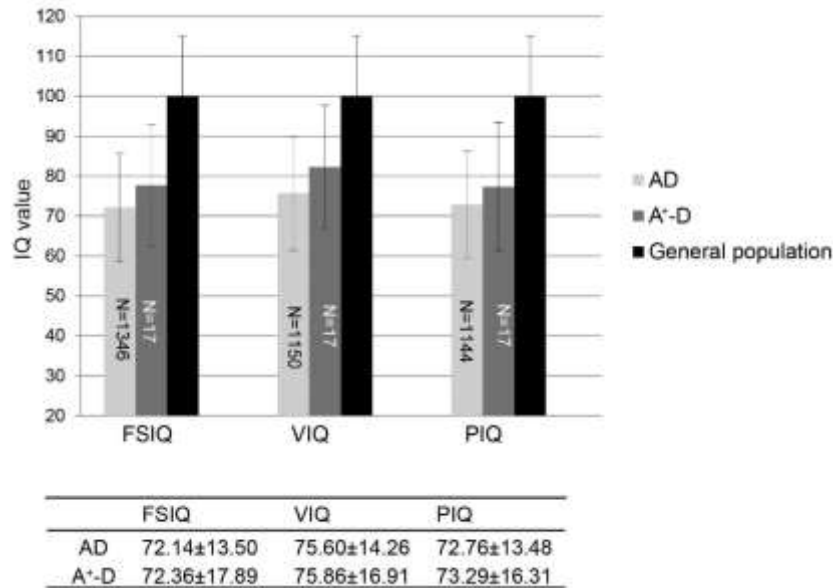
<sup>a</sup>*P* values were calculated for categorical variables from Pearson chi-square software. <sup>b</sup>*P* value was calculated from fisher's exact test, <sup>c</sup>CHD, congenital heart disease, is defined as subjects with Tetralogy of Fallot (TOF), Persistent Truncus Arteriosus (PTA) or Interrupted Aortic Arch Type B (IAAB); <sup>d</sup>Full scale IQ; <sup>e</sup>Verbal IQ, <sup>f</sup>Performance IQ.



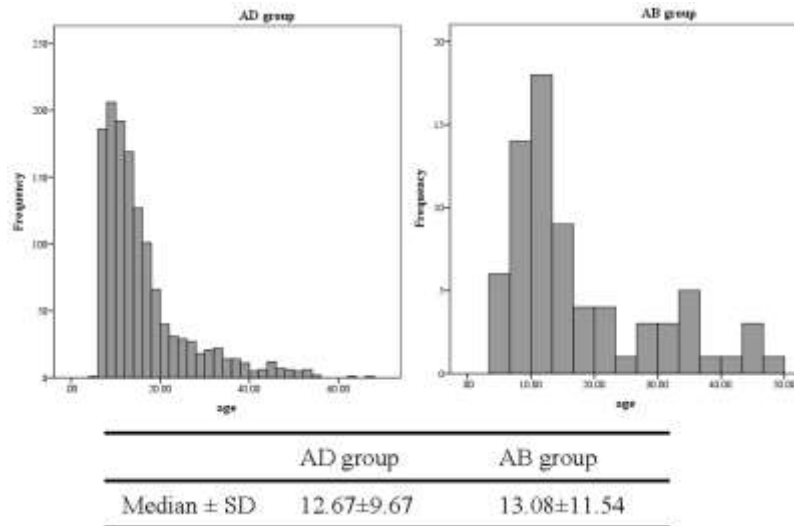
## Supplementary Figures



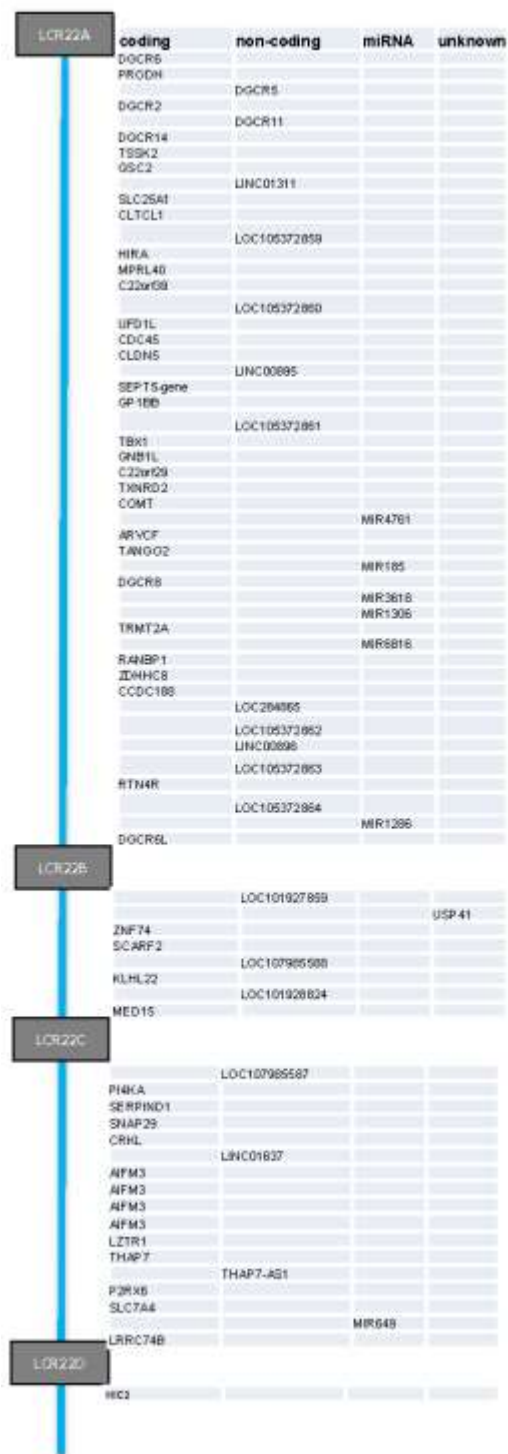
**Supplementary Fig. 1** Flow diagram of selection steps of subjects with 22q11.2 deletion syndrome.



**Supplementary Fig. 2.** IQ differences between subjects with AD and nested A<sup>+</sup>-D (2.8Mb) deletion types. IQ values are expressed as mean±SD. An independent-samples t-test was conducted to compare the mean IQ score in subjects carrying the AD deletion with those carrying A<sup>+</sup>-D within the 22q11.2DS cohort. No significant differences were observed. Numbers in the bars denote samples size of each of the category, test for all three IQ scores have a  $P > 0.05$



**Supplementary Fig. 3.** Distribution of age among subjects with 22q11.2DS with the AD deletion and AB deletion, respectively. The distributions of age in both AD (1,351 subjects) and AB (77 subjects) groups violate the normal distribution assumption according to the one-sample Kolmogorov- Smirnov test (both asymptotic  $P < 0.05$ ), while the distribution is the same between AD and AB groups ( $P > 0.05$  for Mann-Whitney U test). No significant differences were observed for the median ages as indicated by the independent-samples median test ( $P > 0.05$ ). Age is expressed as median  $\pm$ SD



**Supplementary Fig. 4.** Genetic architecture of the 22q11.2 region based on the hg38 genome assembly. Coding genes, non-coding genes, miRNA, unknown genes and pseudogenes were aligned along the 3 Mb 22q11.2 region (chr22:18906222-21451463) spanning the four LCR22s (LCR22A-D), respectively. There are

49 coding genes, 18 non-coding RNAs, 7 miRNAs, 3 pseudogenes and 1 gene that is unclear whether it is a coding gene or pseudogene.